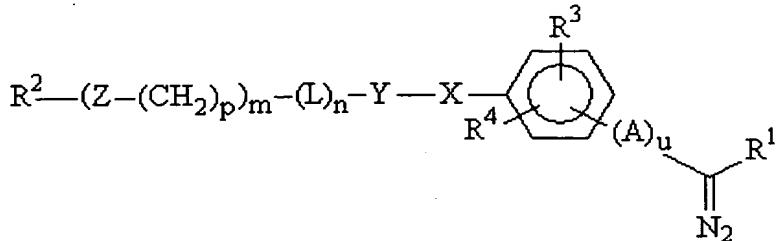


**Amendments to the Claims:**

The following listing of claims will replace all prior versions, and listings, of claims in the application:

26. (New) A temperature-stable labeling reagent of formula (0):



in which:

$R^1$  represents H or an alkyl, aryl or substituted aryl group,

$R^2$  represents a detectable marker or at least two detectable markers interlinked by at least one multimeric structure,

$L$  is a linker arm comprising a linear chain of at least two covalent bonds and  $n$  is an integer equal to 0 or 1,

$R^3$  and  $R^4$  represent, independently of one another: H,  $NO_2$ , Cl, Br, F, I,  $R^2$  -  $(L)_n$ -Y-X-, OR, SR,  $NR_2$ , R, NHCOR, CONHR, COOR, -CO-NH-( $CH_2$ )<sub>3</sub>-(O- $CH_2$ - $CH_2$ )<sub>3</sub>- $CH_2$ -NH-R<sup>2</sup>, -CO-NH-( $CH_2$ )<sub>3</sub>-(O- $CH_2$ - $CH_2$ )<sub>4</sub>- $CH_2$ -NH-R<sup>2</sup> with R = alkyl or aryl,

$A$  is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and  $u$  is an integer between 0 and 2, preferably 0 or 1,

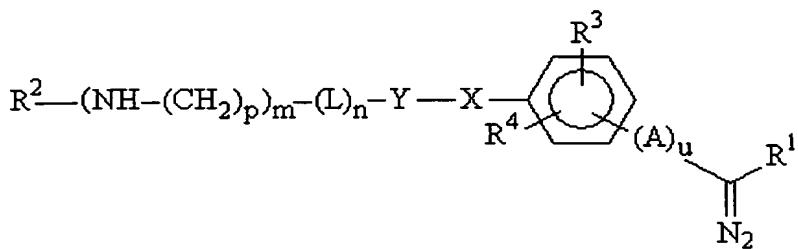
-Y-X- represents -CONH-, -NHCO-, - $CH_2O$ -, - $CH_2S$ -,

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

$m$  is an integer between 1 and 10, preferably between 1 and 3, and

$p$  is an integer between 1 and 10, preferably between 1 and 3.

27. (New) The labeling reagent, as claimed in claim 26, of formula (1):



in which:

$R^1$  represents H or an alkyl, aryl or substituted aryl group,

$R^2$  represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

$L$  is a linker arm comprising a linear chain of at least two covalent bonds and  $n$  is an integer equal to 0 or 1,

$R^3$  and  $R^4$  represent, independently of one another: H,  $NO_2$ , Cl, Br, F, I,  $R^2$  -  $(L)_n-Y-X-$ , OR, SR,  $NR_2$ , R,  $NHCOR$ ,  $CONHR$ ,  $COOR$ , -CO-NH-( $CH_2$ )<sub>3</sub>-(O- $CH_2$ - $CH_2$ )<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-( $CH_2$ )<sub>3</sub>-(O- $CH_2$ - $CH_2$ )<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl, and

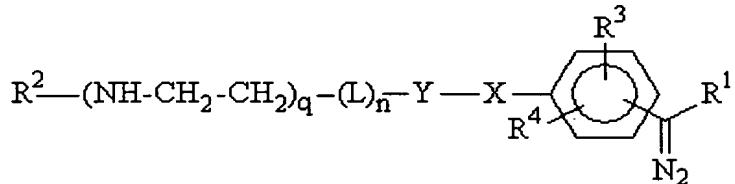
-Y-X- represents -CONH-, -NHCO-, -CH<sub>2</sub>O-, -CH<sub>2</sub>S-,

$m$  is an integer between 1 and 10, preferably between 1 and 3, and

$p$  is an integer between 1 and 10, preferably between 1 and 3.

28. (New) The reagent as claimed in claim 27, wherein  $p$  is less than or equal to  $m$ .

29. (New) The reagent as claimed in claim 27, of formula (2):



in which:

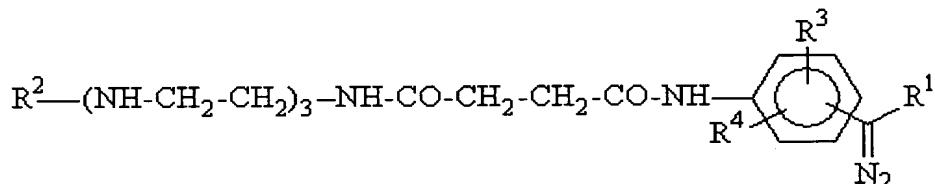
$R^1$  represents H or an alkyl, aryl or substituted aryl group,

$R^2$  represents a detectable label or at least two detectable labels interlinked by means of at least one multimeric structure,

$L$  is a linker arm comprising a linear chain of at least two covalent bonds and  $n$  is an integer equal to 0 or 1,

$R^3$  and  $R^4$  represent, independently of one another: H, NO<sub>2</sub>, Cl, Br, F, I, R<sup>2</sup> - (L)<sub>n</sub>-Y-X-, OR, SR, NR<sub>2</sub>, R, NHCOR, CONHR, COOR, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl, and  $q$  is an integer between 1 and 10, preferably between 1 and 3.

30. (New) The reagent, as claimed in claim 29, of formula (3):



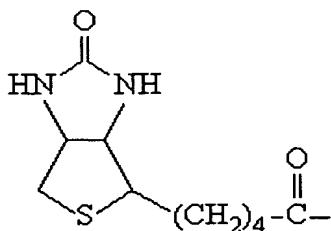
in which:

$R^1$  represents H or an alkyl, aryl or substituted aryl group,

$R^2$  represents a detectable label or at least two detectable labels interlinked by means of at least one multimeric structure,

$R^3$  and  $R^4$  represent, independently of one another: H, NO<sub>2</sub>, Cl, Br, F, I, R<sup>2</sup> - (L)<sub>n</sub>-Y-X-, OR, SR, NR<sub>2</sub>, R, NHCOR, CONHR, COOR, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl.

31. (New) The reagent as claimed in claim 30, wherein  $R^2$  consists of a D-biotin residue of formula (4):



32. (New) The reagent as claimed in claim 31, wherein  $R^1$  consists of:  $CH_3$ , and  $R^3$  and  $R^4$  each represent: H.

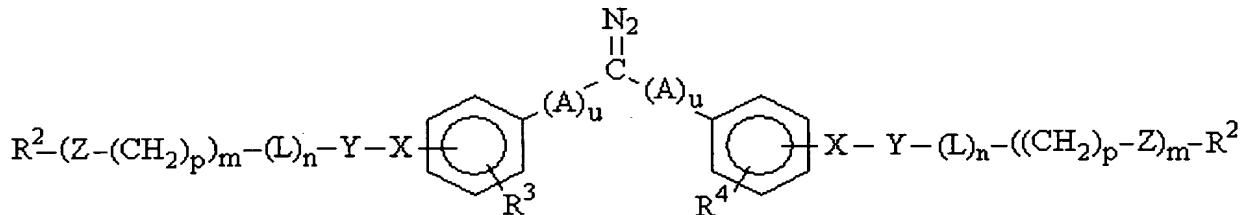
33. (New) The reagent as claimed in claim 29, in which the structure  $-(L)_n-$  consists of:

spermine or  $N,N'$ -bis(3-aminopropyl)-1,4-diaminobutane:  $NH_2-(CH_2)_3-NH-(CH_2)_4-NH-(CH_2)_3-NH_2$ , or

spermidine or  $N$ -(3-aminopropyl)-1,4-butanediamine:  $H_2N-(CH_2)_4-NH-(CH_2)_3-NH_2$ , or

a derivative containing an alanine motif:  $NH_2-CH_2-CH_2-COOH$ .

34. (New) A temperature-stable labeling reagent of formula (6):



in which:

$R^1$  represents H or an alkyl, aryl or substituted aryl group,

$R^2$  represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

$L$  is a linker arm comprising a linear chain of at least two covalent bonds and  $n$  is an integer equal to 0 or 1,

$R^3$  and  $R^4$  represent independently of one another: H,  $NO_2$ , Cl, Br, F, I,  $R^2$  -  $(L)_n-Y-X$ , OR, SR,  $NR_2$ , R,  $NHCOR$ ,  $CONHR$ ,  $COOR$ ,  $-CO-NH-(CH_2)_3-(O-CH_2-CH_2)_3-CH_2-NH-R^2$ ,  $-CO-NH-(CH_2)_3-(O-CH_2-CH_2)_4-CH_2-NH-R^2$  with R = alkyl or aryl,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and u is an integer between 0 and 2, preferably 0 or 1,

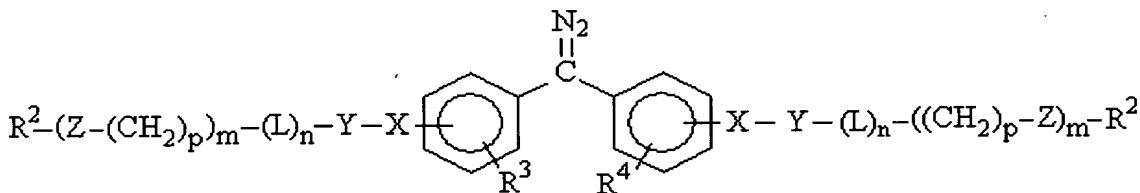
-Y-X- represents -CONH-, -NHCO-, -CH<sub>2</sub>O-, -CH<sub>2</sub>S-,

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

m is an integer between 1 and 10, preferably between 1 and 3, and

p is an integer between 1 and 10, preferably between 1 and 3.

35. (New) The labeling reagent, as claimed in claim 34, of formula (7):



in which:

R<sup>1</sup> represents H or an alkyl, aryl or substituted aryl group,

R<sup>2</sup> represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R<sup>3</sup> and R<sup>4</sup> represent, independently of one another: H, NO<sub>2</sub>, Cl, Br, F, I, R<sup>2</sup> - (L)<sub>n</sub> - Y - X -, OR, SR, NR<sub>2</sub>, R, NHCOR, CONHR, COOR, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH<sub>2</sub>O-, -CH<sub>2</sub>S-,

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

m is an integer between 1 and 10, preferably between 1 and 3, and

p is an integer between 1 and 10, preferably between 1 and 3.

36. (New) The reagent as claimed in claim 26, wherein L comprises a motif -(O-CH<sub>2</sub>-CH<sub>2</sub>)-, repeated from 1 to 20 times, preferably from 1 to 10 times, and even more preferably from 2 to 5 times, -Z- then being represented by -NH-, -NHCO- or -CONH-.

37. (New) The reagent as claimed in claim 34, wherein L comprises a motif -(O-CH<sub>2</sub>-CH<sub>2</sub>)-, repeated from 1 to 20 times, preferably from 1 to 10 times, and even more preferably from 2 to 5 times, -Z- then being represented by -NH-, -NHCO- or -CONH-.

38. (New) A method for the synthesis of a labeling reagent as claimed in claim 26, comprising the following steps:

- a) a label or a label precursor having a reactive function R<sup>6</sup> is provided,
- b) a linker arm of formula (8):



is provided,

in which formula:

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

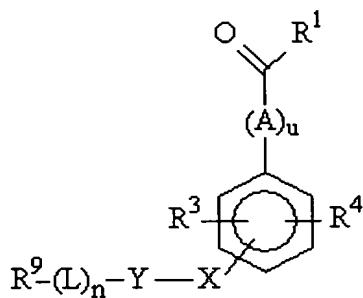
m is an integer between 1 and 10, preferably between 1 and 3,

p is an integer between 1 and 10, preferably between 1 and 3,

R<sup>7</sup> and R<sup>8</sup> represent two reactive functions which may be identical or different,

c) the reactive function R<sup>6</sup> of said label or label precursor and the function R<sup>7</sup> of the linker arm of formula (8) are reacted together in the presence of at least one coupling agent so as to form a covalent bond, R<sup>6</sup> and R<sup>7</sup> being complementary,

- d) a derivative of formula (9):



is provided,

in which formula:

R<sup>1</sup> represents H or an alkyl, aryl or substituted aryl group,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R<sup>3</sup> and R<sup>4</sup> represent, independently of one another: H, NO<sub>2</sub>, Cl, Br, F, I, R<sup>2</sup>-(L)<sub>n</sub>-Y-X-, OR, SR, NR<sub>2</sub>, R, NHCOR, CONHR, COOR, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH<sub>2</sub>O-, -CH<sub>2</sub>S-,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazomethyl function with the aromatic ring and u is an integer equal to 0 or 1, and

R<sup>9</sup> represents a reactive function complementary to R<sup>8</sup>,

e) the reactive function R<sup>9</sup> of the derivative of formula (9) and the function R<sup>8</sup> of the linker arm of formula (8) are reacted together in the presence of at least one coupling agent so as to form a covalent bond,

f) the hydrazine or one of its derivatives is reacted with the ketone or aldehyde function so as to form a hydrazone, and

g) the hydrazone is converted to a diazomethyl function by means of an appropriate treatment.

39. (New) A method for the synthesis of a labeling reagent as claimed in claim 34, comprising the following steps:

- a) a label or a label precursor having a reactive function  $R^6$  is provided,
- b) a linker arm of formula (8):



is provided,

in which formula:

$-Z-$  represents  $-NH-$ ,  $-NHCO-$ ,  $-CONH-$  or  $-O-$ ,

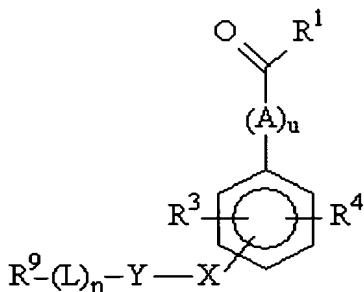
$m$  is an integer between 1 and 10, preferably between 1 and 3,

$p$  is an integer between 1 and 10, preferably between 1 and 3,

$R^7$  and  $R^8$  represent two reactive functions which may be identical or different,

c) the reactive function  $R^6$  of said label or label precursor and the function  $R^7$  of the linker arm of formula (8) are reacted together in the presence of at least one coupling agent so as to form a covalent bond,  $R^6$  and  $R^7$  being complementary,

- d) a derivative of formula (9):



is provided,

in which formula:

$R^1$  represents H or an alkyl, aryl or substituted aryl group,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

$R^3$  and  $R^4$  represent, independently of one another: H,  $NO_2$ , Cl, Br, F, I,  $R^2$  - $(L)_n-Y-X-$ , OR, SR,  $NR_2$ , R,  $NHCOR$ ,  $CONHR$ ,  $COOR$ , -CO-NH-( $CH_2$ )<sub>3</sub>-(O- $CH_2$ - $CH_2$ )<sub>3</sub>- $CH_2$ -NH- $R^2$ , -CO-NH-( $CH_2$ )<sub>3</sub>-(O- $CH_2$ - $CH_2$ )<sub>4</sub>- $CH_2$ -NH- $R^2$  with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, - $CH_2O$ -, - $CH_2S$ -,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazomethyl function with the aromatic ring and u is an integer equal to 0 or 1, and

$R^9$  represents a reactive function complementary to  $R^8$ ,

e) the reactive function  $R^9$  of the derivative of formula (9) and the function  $R^8$  of the linker arm of formula (8) are reacted together in the presence of at least one coupling agent so as to form a covalent bond,

f) the hydrazine or one of its derivatives is reacted with the ketone or aldehyde function so as to form a hydrazone, and

g) the hydrazone is converted to a diazomethyl function by means of an appropriate treatment.

40. (New) The method of synthesis as claimed in claim 38, wherein it comprises:  
an additional step consisting of protection of the ketone or aldehyde function of compound (9), and  
a subsequent additional step consisting of deprotection of said ketone or aldehyde function.

41. (New) The method of synthesis as claimed in claim 39, wherein it comprises:  
an additional step consisting of protection of the ketone or aldehyde function of compound (9), and

a subsequent additional step consisting of deprotection of said ketone or aldehyde function.

42. (New) A method for the labeling of a biological molecule, in particular a nucleic acid, comprising bringing into contact, in homogeneous solution, in a substantially aqueous buffer, a biological molecule and a reagent, obtained as claimed in claim 26.

43. (New) A method for the labeling of a biological molecule, in particular a nucleic acid, comprising bringing into contact, in homogeneous solution, in a substantially aqueous buffer, a biological molecule and a reagent, obtained as claimed in claim 34.

44. (New) A labeled biological molecule which can be obtained by means of the method as claimed in claim 42.

45. (New) A labeled biological molecule which can be obtained by means of the method as claimed in claim 43.

46. (New) A method for the labeling and fragmentation of a single-stranded or double-stranded nucleic acid, comprising the following steps:

fragmenting the nucleic acid,

attaching a label to at least one of the fragments by means of a labeling reagent chosen from the reagents obtained as claimed in claim 26,

said reagent coupling covalently and predominantly on at least one phosphate of said fragment.

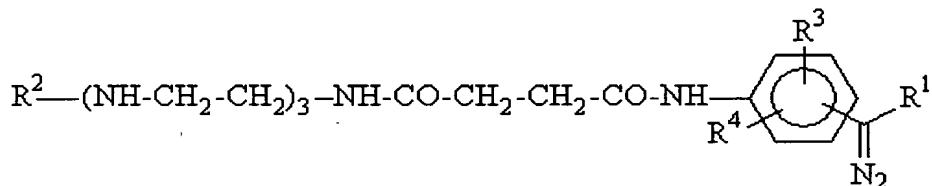
47. (New) A method for the labeling and fragmentation of a single-stranded or double-stranded nucleic acid, comprising the following steps:

fragmenting the nucleic acid,

attaching a label to at least one of the fragments by means of a labeling reagent chosen from the reagents obtained as claimed in claim 34,

said reagent coupling covalently and predominantly on at least one phosphate of said fragment.

48. (New) The method as claimed in claim 46, wherein the labeling reagent is chosen from the compounds of formula (3):



in which:

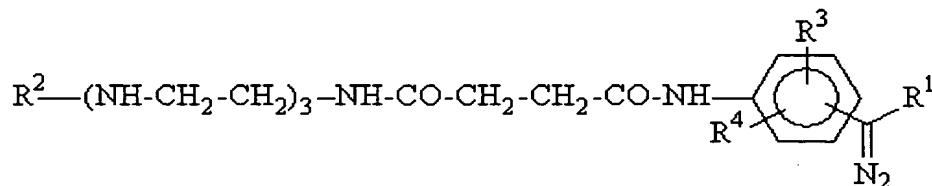
R<sup>1</sup> represents H or an alkyl, aryl or substituted aryl group,

R<sup>2</sup> represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1, and

R<sup>3</sup> and R<sup>4</sup> represent, independently of one another: H, NO<sub>2</sub>, Cl, Br, F, I, R<sup>2</sup> - (L)<sub>n</sub>-Y-X-, OR, SR, NR<sub>2</sub>, R, NHCOR, CONHR, COOR, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl.

49. (New) The method as claimed in claim 47, wherein the labeling reagent is chosen from the compounds of formula (3):



in which:

R<sup>1</sup> represents H or an alkyl, aryl or substituted aryl group,

$R^2$  represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

$L$  is a linker arm comprising a linear chain of at least two covalent bonds and  $n$  is an integer equal to 0 or 1, and

$R^3$  and  $R^4$  represent, independently of one another: H, NO<sub>2</sub>, Cl, Br, F, I,  $R^2$  - (L)<sub>n</sub>-Y-X-, OR, SR, NR<sub>2</sub>, R, NHCOR, CONHR, COOR, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>-NH-R<sup>2</sup>, -CO-NH-(CH<sub>2</sub>)<sub>3</sub>-(O-CH<sub>2</sub>-CH<sub>2</sub>)<sub>4</sub>-CH<sub>2</sub>-NH-R<sup>2</sup> with R = alkyl or aryl.

50. (New) The method as claimed in claim 48, wherein the fragmentation and the labeling are carried out in two steps.

51. (New) The method as claimed in claim 49, wherein the fragmentation and the labeling are carried out in two steps.

52. (New) The method as claimed in claim 48, wherein the fragmentation and the labeling are carried out in one step.

53. (New) The method as claimed in claim 49, wherein the fragmentation and the labeling are carried out in one step.

54. (New) The method as claimed in claim 50, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

55. (New) The method as claimed in claim 52, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

56. (New) The method as claimed in claim 51, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

57. (New) The method as claimed in claim 50, wherein the fragmentation is carried out by an enzymatic, physical or chemical process.

58. (New) The method as claimed in claim 51, wherein the fragmentation is carried out by an enzymatic, physical or chemical process.

59. (New) A labeled nucleic acid which can be obtained by means of the method as claimed in claim 46.

60. (New) A labeled nucleic acid which can be obtained by means of the method as claimed in claim 47.

61. (New) A kit for the detection of a target nucleic acid, comprising a labeled nucleic acid as claimed in claim 59.

62. (New) A kit for the detection of a target nucleic acid, comprising a labeled nucleic acid as claimed in claim 60.

63. (New) A solid support to which is attached a reagent as claimed in claim 26.

64. (New) A solid support to which is attached a reagent as claimed in claim 34.

65. (New) A method for the capture of nucleic acids, comprising the following steps:

providing a solid support to which is directly or indirectly attached at least one biological molecule as claimed in claim 44, the biological molecule or the nucleic acid comprising a diazomethyl function,

bringing into contact a biological sample which may contain free nucleic acids, and

washing the solid support where the molecule(s) is (are) covalently attached at least to a nucleic acid.

66. (New) A method for the capture of nucleic acids, comprising the following steps:

providing a solid support to which is directly or indirectly attached at least one biological molecule as claimed in claim 45, the biological molecule or the nucleic acid comprising a diazomethyl function,

bringing into contact a biological sample which may contain free nucleic acids,  
and

washing the solid support where the molecule(s) is (are) covalently attached at  
least to a nucleic acid.